ORGANOMETALLICS

ARTICLE

pubs.acs.org/Organometallics

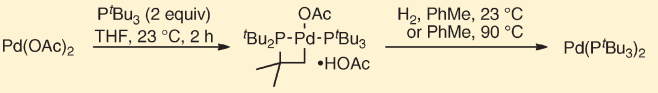
Characterization, Reactivity, and Potential Catalytic Intermediacy of a Cyclometalated Tri-*tert*-butylphosphine Palladium Acetate Complex

William H. Henderson, Jimmy M. Alvarez, Chad C. Eichman, and James P. Stambuli*

Department of Chemistry, The Ohio State University, 100 W. 18th Avenue, Columbus, Ohio 43210, United States

Supporting Information

ABSTRACT: Palladium acetate and tri-*tert*-butylphosphine react at room temperature via C−H activation of a *tert*-butyl group to form the novel palladium(II) complex [(P^tBu_3)Pd-($CH_2C(CH_3)_2P^tBu_2$)(OAc)]. This cyclometalated complex can be reduced to $Pd(P^tBu_3)_2$ by either heat or hydrogen, but is resistant to reduction by alkoxide bases and amines. As a result of the existence of this cyclometalated complex, the production of catalytically active palladium(0) species generated in situ from $Pd(OAc)_2$ and tri-*tert*-butylphosphine is diminished, as evident by the catalytic inactivity of this complex. Additionally, datively bound tri-*tert*-butylphosphine is easily displaced by amines and less basic phosphines to form a series of novel cyclometalated palladium(II) complexes.



INTRODUCTION

The development and application of palladium-catalyzed cross-coupling reactions is a dominant area of research in synthetic chemistry. The utility of these classes of reactions was punctuated in 2010 with the awarding of the Nobel Prize in Chemistry to three pioneers in cross-coupling chemistry, Richard Heck, Ei-ichi Negishi, and Akira Suzuki.[1] At the forefront of the advancement of these reactions was the discovery that the combination of palladium salts and bulky, electron-rich trialkylphosphines created highly unsaturated and reactive catalysts.[2] One of the first widely applicable bulky, electron-rich ligands was tri-*tert*-butylphosphine (P^tBu_3). The increased activity of P^tBu_3 is highlighted by its ability to form stable unsaturated T-shaped monomeric palladium complexes, which are proposed as catalytic intermediates in many reactions.[3] In 1997, the Tosoh Corporation reported that $Pd(dba)_2$ (dba = dibenzylideneacetone) or $Pd(OAc)_2$, when used with P^tBu_3, effectively catalyzes the amination of aryl halides with piperazines.[4] More recently Hartwig and co-workers have expanded the scope of palladium-catalyzed reactions using P^tBu_3 in aryl aminations[5] as well as α-arylations of carbonyls[6] and nitriles.[7] Additionally, Fu and co-workers have shown that P^tBu_3 and a palladium salt effectively catalyze Suzuki−Miyaura,[8] Negishi,[9] Heck,[10] Sonogashira,[11] and Stille[12] cross-coupling reactions with aryl bromides and aryl chlorides.[13]

Most of the catalytic cycles proposed in palladium-catalyzed cross-coupling reactions are believed to operate on a Pd(0)/Pd(II) platform. The most popular starting palladium precatalysts are $Pd(dba)_2$ and $Pd(OAc)_2$, as they are readily available or easily prepared, and are stable to air and moisture. The widespread use of $Pd(dba)_2$ as a precatalyst is interesting because of the ability of dba to deleteriously affect a reaction outcome.[14] Moreover, the actual composition of $Pd(dba)_2$ is subject to preparatory method of choice, can vary from batch to batch, and is difficult to quantify its purity spectroscopically. However, $Pd(dba)_2$ provides a more direct route to generating a desired palladium catalyst than $Pd(OAc)_2$ because one can imagine that a mixture of $Pd(dba)_2$ and externally added phosphine react together and the weaker dba ligand is replaced at the metal by the phosphine. The second dba ligand can then be displaced by another phosphine or by the incoming substrate.[15] Moreover, the oxidation state at palladium goes unchanged upon addition of ligand, and once the catalyst is formed, oxidative addition can occur, resulting in a change in oxidation state from Pd(0) to Pd(II). The formation of palladium catalysts from $Pd(OAc)_2$ is not as straightforward in this regard. From a structural standpoint, palladium acetate is well-defined;[16] however, the oxidation state of $Pd(OAc)_2$ is Pd(II), and the mode of reduction to Pd(0) upon addition of phosphine is still unclear in many cases.[17] Typically, no intermediate palladium species are isolated during these reductions, and studies relating to the reduction of $Pd(OAc)_2/P^tBu_3$ combinations have not been reported.

If one charges 5 mol % of $Pd(OAc)_2$ and a corresponding ligand into a cross-coupling reaction, the intermediate reactions that follow are unlikely to produce the active catalytic species with quantitative conversion. Therefore, the identification of intermediate complexes during these transformations is important to understand how to more cleanly generate a complex that better resembles the active catalyst,[18] while avoiding any potential reactions that unproductively consume $Pd(OAc)_2$ and ligand. The identification and isolation of these complexes may help to design catalysts that allow a decreased catalyst loading and increased catalyst turnover. We now report the isolation and reactivity of one of these complexes: a cyclometalated complex formed from the facile C−H insertion of $Pd(OAc)_2$ with P^tBu_3 at room temperature (Scheme 1).

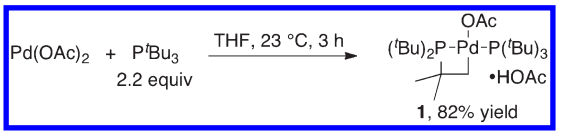
RESULTS AND DISCUSSION

While repeating a procedure using a catalyst formed from five equivalents of P^tBu_3 and one equivalent of $Pd(OAc)_2$, employing

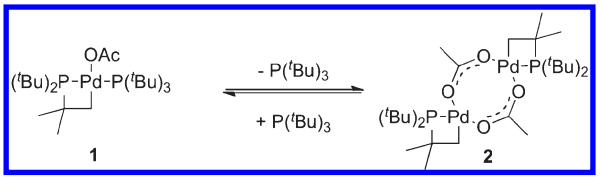
Received: July 27, 2011
Published: August 25, 2011

dx.doi.org/10.1021/om2006936 | *Organometallics* 2011, 30, 5038–5044

Scheme 1



Scheme 2



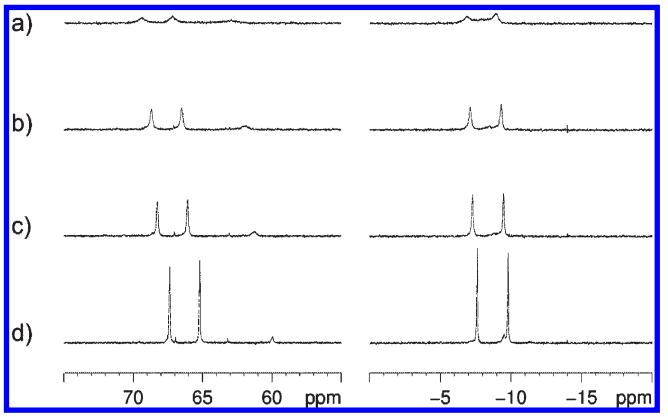


Figure 1. Variable-temperature ^{31}P NMR spectra of palladacycle **1**: (a) 33 °C, (b) 16 °C, (c) 6 °C, (d) −14 °C.

a smaller amount of expensive P^{t}Bu$_3$ was desired. Moreover, it was unclear what the identity of the product of this reaction would be. Initially, one would expect Pd(P^{t}Bu$_3$)$_2$ to somehow form. The formation of this Pd(0) complex could arise from the generation of Pd[(P^{t}Bu$_3$)$_2$(OAc)$_2$], which further reacts to form Pd(P^{t}Bu$_3$)$_2$. However, the existence of metal complexes containing two bulky P^{t}Bu$_3$ ligands on a single palladium center is rare.[19] A quick investigation of this reaction by ^{31}P NMR spectroscopy did not show any evidence of the diacetate complex or Pd(P^{t}Bu$_3$)$_2$. A large signal corresponding to uncoordinated P^{t}Bu$_3$ at 63.1 ppm was observed along with broad signals near 68.1 and −8.0 ppm. The downfield resonances nearer to uncomplexed P^{t}Bu$_3$ are in the area of datively bound P^{t}Bu$_3$, while P^{t}Bu$_3$ resonances upfield from 0 ppm typically correspond to cyclometalated phosphines. Therefore, it was believed that there were at least two distinct complexes present in this reaction.

Repeating the reaction using two equivalents of P^{t}Bu$_3$ produced the same resonances in the ^{31}P NMR spectrum, less the free phosphine peak at 63.1 ppm. Crystallization of the crude reaction mixture from pentane unexpectedly provided the single novel complex [(P^{t}Bu$_3$)Pd(CH$_2$C(CH$_3$)$_2$P^{t}Bu$_2$)(OAc)]HOAc (**1**), in 81% yield, resulting from insertion into the C−H bond of P^{t}Bu$_3$ and formation of AcOH. Because complex **1** was formed from mixing P^{t}Bu$_3$ and Pd(OAc)$_2$ at room temperature, it functions either as a precatalyst to the active catalytic species or as a product of the catalyst deactivation pathway and may

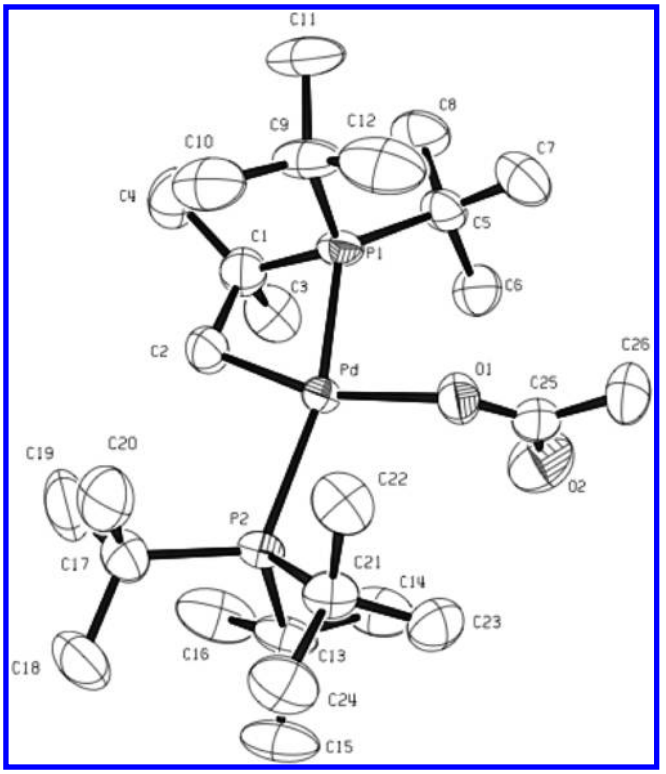


Figure 2. ORTEP diagram of complex **1**. Thermal ellipsoids are set at 50% probability. Selected bond lengths [Å] and angles [deg]: Pd−P1 2.2795(7); Pd−C2 2.066(3); Pd−O1 2.156(2); C2−Pd−O1 162.35(11); P1−Pd−P2 167.01(3); C1−P1−Pd 88.32 (11).

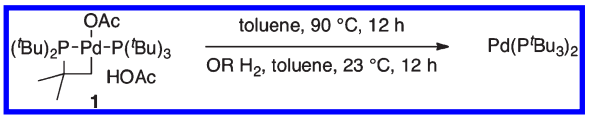
provide insight into how Pd(OAc)$_2$ is reduced to Pd(0) in cross-coupling reactions that employ P^{t}Bu$_3$ as a ligand.

The seemingly complex ^{31}P NMR spectrum is caused by the equilibrium of **1** and known dimeric complex **2** (Scheme 2).[7,20] At −14 °C the broad resonances in the ^{31}P NMR and ^{1}H NMR spectra coalesce to form two sharp, distinct signals that correspond to datively bound P^{t}Bu$_3$ at 68.1 ppm and the cyclometalated P^{t}Bu$_3$, which appears at −8.0 ppm (Figure 1). If one equivalent of P^{t}Bu$_3$ is added to Pd(OAc)$_2$, the known cyclometalated palladium dimer **2** is formed in situ and is identified by a broad resonance at −8.9 ppm. Addition of another equivalent of P^{t}Bu$_3$ causes dimer **2** to dissociate, forming complex **1**. Any additional P^{t}Bu$_3$ remains as free ligand exchanging with bound P^{t}Bu$_3$, noted by the broad signal at 63.1 ppm. Complex **1** formed directly from Pd(OAc)$_2$ and P^{t}Bu$_3$ contained coordinated acetic acid and was used for subsequent studies; however, complex **1** less the coordinated acetic acid could be prepared from isolated complex **2** and P^{t}Bu$_3$.

An X-ray crystal structure of complex **1** was obtained (Figure 2). The geometry about the palladium center is distorted square planar with C(2)−Pd−O(1) and P(1)−Pd−P(2) bond angles of 162.3° and 167.0°, respectively. The cyclometalated phosphine has a bite angle of 68.3°, slightly more strained than observed in the previously reported X-ray crystal structure of the cyclometalated dimer bis(μ-chloro)bis[2-(di-*tert*-butylphosphino)-2-methylpropyl]dipalladium,[21] which has a bite angle of 70.0°. The Pd−C(2) and Pd−P(1) bond lengths are 2.066 and 2.279 Å, respectively, compared to 2.052 and 2.209 Å in bis(μ-chloro)bis[2-(di-*tert*-butylphosphino)-2-methylpropyl]dipalladium. The Pd−O(1) bond is 2.156 Å, slightly elongated compared to

dx.doi.org/10.1021/om2006936 |*Organometallics* 2011, 30, 5038–5044

Scheme 3



the known Herrmann−Beller palladacycle with bridging acetates, which have Pd−O bond distances of 2.147 and 2.111 Å.[22]

In order to better understand how complex **1** may function as a catalyst precursor, we attempted to affect its reduction to Pd(0) by adding bases typically utilized in cross-coupling reactions. In THF at 23 °C, K_2CO_3, Cs_2CO_3, K_3PO_4, and NaOAc do not promote reduction to Pd(0) as observed by ^{31}P NMR spectroscopy. Interestingly, the addition of NaO^{t}Bu created a new unidentifiable complex with a sharp ^{31}P NMR signal at −2.4 ppm and free P^{t}Bu$_3$. All attempts to isolate this complex were unsuccessful. This complex could potentially be formed via *tert*-butoxide coordinating to palladium, displacing either the acetate, P^{t}Bu$_3$, or both.

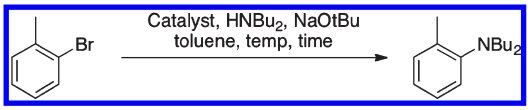
Complex **1** was then submitted directly to a hydrogen atmosphere, since hydrogenations have been reported with Pd(OAc)$_2$ and excess P^{t}Bu$_3$ in the presence of formic acid in THF.[23] Interestingly, when complex **1** is stirred in either THF or toluene at 23 °C under a hydrogen atmosphere, it was cleanly converted to Pd(P^{t}Bu$_3$)$_2$ in 12 h. Further investigations into the reactivity of complex **1** showed that in the presence of O_2 and air the complex decomposes, forming tri-*tert*-butylphosphine oxide and minor amounts of unidentified products. Not surprisingly, complex **1** is unreactive toward aryl bromides and aryl iodides at room temperature.

Since many reactions containing Pd(OAc)$_2$/P^{t}Bu$_3$ combinations require elevated temperatures, we postulated that thermal decomposition to Pd(0) might be possible. Complex **1** is stable in toluene at 23 °C for days; however, when heated to 90 °C, it decomposes within 12 h to form Pd(P^{t}Bu$_3$)$_2$. If alternatively prepared Pd(P^{t}Bu$_3$)$_2$ was stirred with four equivalents of AcOH at 23 °C, complex **1** was not observed.

To study the reactivity of complex **1** in cross-coupling reactions, we submitted **1** to previously reported reaction conditions that do not require elevated temperatures, thus preventing thermal decomposition to Pd(0) complexes. Hartwig has shown that Pd(OAc)$_2$ and 0.8 equivalent of P^{t}Bu$_3$ catalyze the amination of *ortho*-substituted aryl bromides at room temperature.[5] We submitted complex **1**, cyclometalated dimer **2**, and Pd(P^{t}Bu$_3$)$_2$ to the reported reaction conditions using 2-bromotoluene and dibutylamine (Table 1). Surprisingly, all three complexes gave poor yields of *N*,*N*-dibutyl-*o*-toluidine. These reactions were then repeated at 60 and 110 °C. At 60 °C, the reaction proceeds in higher yields and faster reaction times for all complexes; however, none of the complexes catalyzed the reaction in yields comparable to reported conditions. At 110 °C, yields and reaction times suffer, perhaps due to rapid catalyst decomposition. It is possible that the active catalyst contains fewer equivalents of P^{t}Bu$_3$ compared to Pd since a higher metal to ligand ratio was more competent at catalyzing these reactions.

To identify the active catalyst in Hartwig's aryl amination reactions, Pd(OAc)$_2$ and P^{t}Bu$_3$ (0.8 equiv) were stirred in toluene for 1 h. The ^{31}P NMR spectrum showed an unidentified resonance at −11.3 ppm and resonances corresponding to **2**. Attempts to isolate the source of the signal at −11.3 ppm were

Table 1. Aryl Aminations of 2-Bromotoluene Using 1, 2, and Pd(P^{t}Bu$_3$)$_2$



entry	catalyst	temp (°C)	time (h)	yield[a]
1	Pd(OAc)$_2$/P^{t}Bu$_3$	23	6	81%[b]
2	complex **1**	23	6	6%
3	complex **2**	23	6	8%
4	Pd(P^{t}Bu$_3$)$_2$	23	6	6%
5	complex **1**	60	3	34%
6	complex **2**	60	3	33%
7	Pd(P^{t}Bu$_3$)$_2$	60	3	30%
8	complex **1**	110	15 min	20%
9	complex **2**	110	15 min	24%
10	Pd(P^{t}Bu$_3$)$_2$	110	15 min	19%

[a] All yields are an average of two 0.25 mmol reactions. Yields were determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard. [b] Reported literature yield.[5]

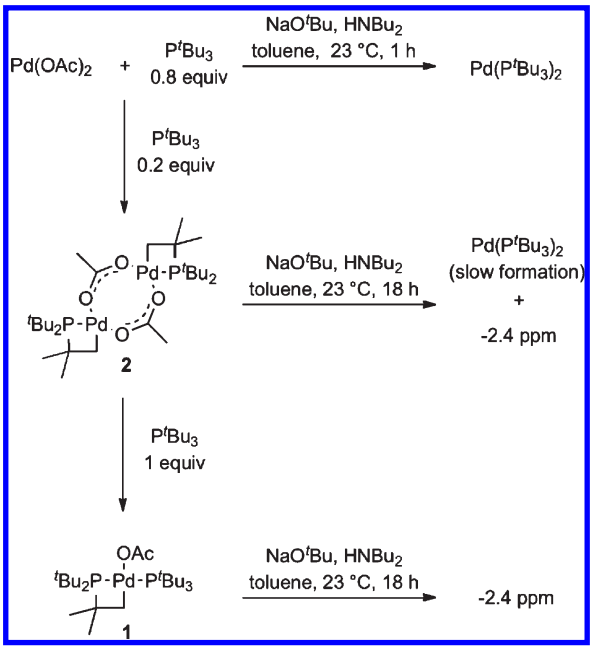
unsuccessful, and likely this unidentified complex plays an important role in generating the active catalyst. If five equivalents of NaO^{t}Bu are added to complex **1** or complex **2**, a resonance at −2.4 ppm appears, indicating formation of the unknown complex. Surprisingly, if Pd(OAc)$_2$, 0.8 equivalent of P^{t}Bu$_3$, and five equivalents of NaO^{t}Bu are stirred together in toluene, a resonance at −2.4 ppm appears as well as a much smaller resonance at 85.7 ppm corresponding to Pd(P^{t}Bu$_3$)$_2$. If the complex at −2.4 ppm was generated in situ by addition of 2.2 equivalents of NaO^{t}Bu to complex **2** in toluene and submitted to the amination conditions at 23 °C, *N*,*N*-dibutyl-*o*-toluidine was produced in a 30% yield.

Secondary and tertiary amines are known to promote the reduction of Pd(OAc)$_2$ to Pd(0) when used in conjunction with alkoxide bases.[17c] Indeed, when Pd(OAc)$_2$, 0.8 equivalent of P^{t}Bu$_3$, five equivalents of NaO^{t}Bu, and HNBu$_2$ are stirred in toluene, the only phosphine resonance present is at 85.7 ppm, indicating formation of Pd(P^{t}Bu$_3$)$_2$. If five equivalents of NaO^{t}Bu, HNBu$_2$, and either complex **1** or complex **2** are stirred together in toluene, initially, only a very small amount of Pd(P^{t}Bu$_3$)$_2$ is seen along with a large signal at −2.4 ppm. After 18 h at room temperature, complex **1** showed only a small amount of Pd(P^{t}Bu$_3$)$_2$ by ^{31}P NMR spectroscopy, while complex **2** continues to slowly form Pd(P^{t}Bu$_3$)$_2$. The low yields of arylamines combined with the ability of complex **1** to withstand conditions that would typically reduce Pd(II) sources to Pd(0) lead to the conclusion that complex **1** is not an intermediate that leads to formation of the active catalyst under these conditions. Instead, complex **1** is likely a product along the catalyst decomposition pathway.

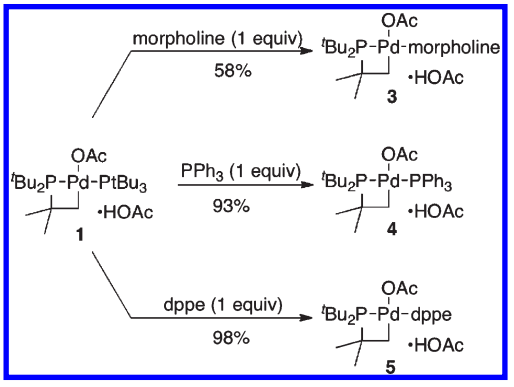
Because complex **1** is able to withstand reduction to Pd(0) in the presence of amines, we chose to examine whether secondary amines were unreactive toward complex **1** or potentially formed new complexes, preventing reduction to Pd(0). The addition of morpholine to complex **1** results in displacement of coordinated P^{t}Bu$_3$, forming a new cyclometalated complex rather than a Pd(0) species. The morpholine-containing complex **3** was

dx.doi.org/10.1021/om2006936 |*Organometallics* 2011, 30, 5038–5044

Scheme 4



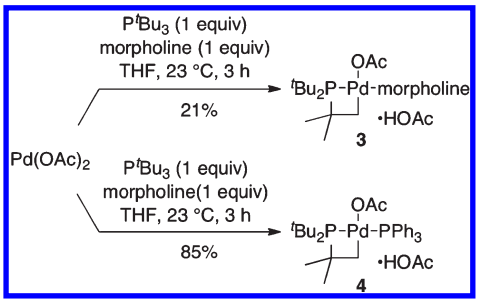
Scheme 5



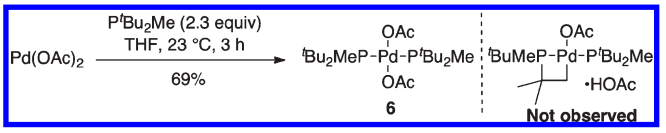
isolated by recrystallization from pentane in 58% yield. We hypothesized that because of the bulkiness of P^tBu_3 at the palladium center, this ligand could also be displaced by smaller, less basic phosphines. Indeed, the addition of PPh_3 to **1** readily displaces P^tBu_3 after 2 h at 23 °C to form the PPh_3-ligated complex **4** in 93% yield. Spectroscopically, complex **4** is well-defined in the ^{31}P NMR spectrum, which shows two sharp doublets at 23 °C. Other phosphines such as 1,2-bis-(diphenylphosphino)ethane (dppe) are also able to displace P^tBu_3, forming the corresponding complex **5** in 98% yield. Complexes **3** and **4** are alternatively formed from the addition of one equivalent of P^tBu_3 and one equivalent of PPh_3 or morpholine, respectively, in THF to a stirring solution of Pd-$(OAc)_2$. The addition of dppe and P^tBu_3 to $Pd(OAc)_2$ primarily forms previously reported $(dppe)_2Pd(OAc)_2$.[24]

Recently, P^tBu_2Me has seen expanded use as a ligand in cross-coupling reactions.[25] While P^tBu_2Me is similar to P^tBu_3 electronically, it has a significantly smaller cone angle (161° for P^tBu_2Me vs 182° for P^tBu_3), and when 2.3 equivalents are stirred with $Pd(OAc)_2$ in THF for 2 h, no cyclometalated complexes

Scheme 6



Scheme 7



resulting from C−H activation are seen. Instead, previously unreported $Pd[(P^tBu_2Me)_2(OAc)_2]$ (**6**) is formed in 69% yield, which may lend insight into the steric requirements for facile C−H activation. Indeed, some complexes containing bulky P^tBu_3 show an agostic C−H interaction that may allude to a low barrier of activation toward cyclometalation.[3] Additionally, the inability of P^tBu_2Me to form stable cyclometalated complexes with $Pd(OAc)_2$ may explain enhanced yields in certain cross-coupling reactions when P^tBu_2Me was used instead of P^tBu_3.[25c,d,26]

Cyclometalated complexes are reported in the literature and occasionally lead to highly reactive catalysts, such as allylic substitutions catalyzed by iridium and a cyclometalated phosphoramidite ligand.[27] In contrast, the results provided herein indicate that complex **1** is likely a catalyst decomposition product at room temperature, unable to form Pd(0) species in catalytically useful amounts. However, prior to cyclometalation, Pd-$(OAc)_2$ in the presence of NaO^tBu, dibutylamine, and P^tBu_3 is readily reduced to Pd(0). Moreover, the stability of complex **1** is demonstrated in its ability to withstand reduction to Pd(0) under conditions that reduce $Pd(OAc)_2/P^tBu_3$ and complex **2** to $Pd(P^tBu_3)_2$, a Pd(0) species.

The analysis and identification of catalyst decomposition pathways is often overlooked and understudied. However, the importance in identifying such species lies in the ability to engineer long-lived catalysts that avoid rapid decomposition pathways. For example, it is common in the literature to find procedures in which a metal salt and ligand are premixed, prior to the addition of substrate and other reactants, to effectively form a catalyst precursor or the active catalyst.[26,28] However, if Pd-$(OAc)_2$ and two equivalents of P^tBu_3 are premixed, reactions may proceed slowly or not at all at room temperature, thus requiring elevated temperatures in order to effectively catalyze reactions. Procedurally, since the cyclometalation of $Pd(OAc)_2$ and P^tBu_3 occurs at room temperature, it would be pertinent to avoid combining $Pd(OAc)_2$ and P^tBu_3 in solution without base or a combination of amine and base present. Furthermore, the stoichiometry of $Pd(OAc)_2$ to P^tBu_3 must be considered. In many cases the optimal stoichiometry of P^tBu_3 to $Pd(OAc)_2$ is less than 2:1, with greater amounts of P^tBu_3 requiring higher

dx.doi.org/10.1021/om2006936 |*Organometallics* 2011, 30, 5038–5044

temperatures.[2,5,29] The ability of **1** to thermally decompose to a zerovalent palladium species should also be noted. While triarylphosphine ligands readily form Pd(0) complexes from Pd(OAc)$_2$, even at room temperature, it would be worthwhile to identify a bulky electron-rich trialkylphosphine ligand that would readily form a zerovalent palladium complex from Pd(OAc)$_2$ without the addition of external reagents.

CONCLUSION

In conclusion we have demonstrated that Pd(OAc)$_2$ and P^{t}Bu$_3$, which are commonly used in cross-coupling reactions, form the novel palladacyclic complex **1** through a facile C−H insertion step at room temperature. The formation of this complex prevents quantitative formation of the precatalyst to the active Pd(0) species. This C−H insertion is likely due to the pronounced steric nature of P^{t}Bu$_3$, as P^{t}Bu$_2$Me, another electron-rich trialkylphosphine, does not form cyclometalated products with Pd(OAc)$_2$ at room temperature. With respect to aminations of *ortho*-substituted aryl bromides, palladacycle **1** is catalytically active. However, **1** appears to move further away from the predominant active catalytic species, as reactions conducted with this complex are slower and significantly lower yielding than reactions using an in situ generated catalyst from Pd(OAc)$_2$ and P^{t}Bu$_3$. While complex **1** is stable to reduction in the presence of amine and base, we have shown that it may be reduced to Pd(P^{t}Bu$_3$)$_2$ with heat or hydrogen. The ability of **1** to form Pd(0) complexes at elevated temperatures provides an avenue for entry into general Pd(0)/Pd(II) catalysis. Typically, strongly coordinating P^{t}Bu$_3$ is easily displaced from palladacycle **1** by smaller, more weakly binding nitrogen- and phosphorus-containing ligands. Utilizing the ability to easily displace P^{t}Bu$_3$, we have prepared a series of novel cyclometalated complexes. Currently, attempts to isolate and identify the aforementioned unidentified complexes are underway in our laboratory.

EXPERIMENTAL SECTION

General Methods. Unless stated otherwise, reactions were conducted in 4 mL borosilicate glass vials under an inert atmosphere. Complex **2** was prepared according to a known literature procedure.[1] Palladium acetate was purified by recrystallization from hot benzene. Morpholine was distilled over calcium hydride. As per literature procedure, dibutylamine was used as received and not dried prior to use in amination reactions.[7] All other commercially obtained reagents were used as received. Thin-layer chromatography (TLC) was conducted with Sorbent Technologies silica gel UV254 precoated plates (0.25 mm) and visualized using UV lamps and anisaldehyde staining. ^{1}H and ^{31}P NMR spectra were recorded on Bruker spectrometers and are reported relative to solvent. IR spectra were recorded on a Perkin-Elmer 1600 FT-IR spectrometer. Elemental analyses were obtained from Robertson Microlit Laboratories.

[(P^{t}Bu$_3$)Pd(CH$_2$C(CH$_3$)$_2$P^{t}Bu$_2$)(OAc)]HOAc (1). Tri-*tert*-butylphosphine (P^{t}Bu$_3$) (230 mg, 1.14 mmol) was added to a stirring solution of Pd(OAc)$_2$ (116 mg, 0.517 mmol) in THF (1 mL) at 23 °C. The solution was stirred for 2 h. The solvent was removed under reduced pressure, and the resulting pale yellow solid dissolved in a minimal amount of pentane before filtering over Celite. The resulting solution was reduced under vacuum until solid formation began and then placed at −30 °C overnight to promote crystal formation. The product was isolated by vacuum filtration, washing with cold pentane to give [(P^{t}Bu$_3$)Pd(CH$_2$C(CH$_3$)$_2$P^{t}Bu$_2$)(OAc)]HOAc (263 mg, 0.418 mmol, 81%) as pale yellow needles. FTIR (film, cm^{-1}): 2900, 2478, 1736, 1707, 1570, 1410, 1271, 1172, 1021, 806. ^{1}H NMR (C$_7$D$_8$, 400 MHz): δ 13.85 (s, 1H), 2.05 (s, 6H), 1.47−1.12 (m, 53H). ^{31}P NMR (C$_7$D$_8$, 162 MHz, 23 °C): δ 67.3, 67.2, 62.9, 6.9, 8.9. ^{31}P NMR (C$_7$D$_8$, 162 MHz, −20 °C): δ 66.3 (d, J = 354 Hz), −8.7 (d, J = 354 Hz). Anal. Calcd for C$_{28}$H$_{60}$O$_4$P$_2$Pd: C, 53.45; H, 9.61. Found: C, 53.53; H, 9.52.

[(C$_4$H$_9$NO)Pd(CH$_2$C(CH$_3$)$_2$P^{t}Bu$_2$)(OAc)]HOAc (3). Method A. To a 4 mL borosilicate glass vial charged with Pd(OAc)$_2$ (92 mg, 0.40 mmol), tri-*tert*-butylphosphine (83 mg, 0.41 mmol, 1.0 equiv), and morpholine (36 μL, 0.41 mmol, 1.0 equiv) was added THF (2 mL). The reaction mixture was stirred at ambient temperature for 2 h. The solvent was removed under reduced pressure, and the yellow solid dissolved in a minimal amount of pentane. The solution was then filtered through a pad of Celite and placed at −30 °C for 12 h. The product was isolated by vacuum filtration, washing with cold pentane to give [(C$_4$H$_9$NO)Pd(CH$_2$C(CH$_3$)$_2$P^{t}Bu$_2$)(OAc)]HOAc (44 mg, 0.086 mmol, 21%) as an off-white crystalline solid.

[(C$_4$H$_9$NO)Pd(CH$_2$C(CH$_3$)$_2$P^{t}Bu$_2$)(OAc)]HOAc (3). Method B. To a 4 mL borosilicate glass vial charged with complex **1** (70 mg, 0.11 mmol) were added morpholine (10 μL, 0.11 mmol, 1.1 equiv) and THF (1 mL). The reaction mixture was stirred at ambient temperature for 2 h. The solvent was removed under reduced pressure. The resulting white solid was dissolved in pentane, and the solution was placed at −30 °C for 12 h. The product was isolated by vacuum filtration, washing with cold pentane to give [(C$_4$H$_9$NO)Pd(CH$_2$C(CH$_3$)$_2$P^{t}Bu$_2$)(OAc)]HOAc (34 mg, 0.07 mmol, 58%) as a white crystalline solid.

Additionally the morpholine complex was prepared less the coordinated acetic acid as follows. **[(C$_4$H$_9$NO)Pd(CH$_2$C(CH$_3$)$_2$P^{t}Bu$_2$)(OAc)]**: To complex **2** (112 mg, 0.15 mmol) in THF (1 mL) was added morpholine (26.0 μL, 0.30 mmol, 2 equiv). The reaction was stirred for 2 h at ambient temperature. The solvent was removed under reduced pressure, and the off-white solid dissolved in a minimal amount of pentane. The crude solution was then filtered through a pad of Celite, and the solution placed at −30 °C for 12 h. The product was isolated by vacuum filtration, washing with cold pentane to give [(C$_4$H$_9$NO)Pd(CH$_2$C(CH$_3$)$_2$P^{t}Bu$_2$)(OAc)] (61 mg, 0.13 mmol, 44%) as a white crystalline solid. FTIR (film, cm^{-1}): 3014, 2960, 1580, 1385, 1179, 1105, 1040, 887, 662. ^{1}H NMR (C$_6$D$_6$, 400 MHz): δ 3.46 (t, J = 4.4 Hz, 4H), 2.64 (s, 4H), 2.16 (s, 3H), 1.36 (d, J = 13.6 Hz, 18H), 1.24 (d, J = 13.6 Hz, 6H), 0.55 (d, J = 0.4 Hz, 2H). ^{31}P NMR (C$_6$D$_6$, 162 MHz): δ −6.7;. Anal. Calcd for C$_{18}$H$_{38}$NO$_3$PPd: C, 47.63; H, 8.44. Found: C, 46.71; H, 7.51.

[(PPh$_3$)Pd(CH$_2$C(CH$_3$)$_2$P^{t}Bu$_2$)(OAc)]HOAc (4). Method A. To a 4 mL borosilicate glass vial charged with Pd(OAc)$_2$ (103 mg, 0.46 mmol), tri-*tert*-butylphosphine (93 mg, 0.46 mmol, 1.0 equiv), and triphenylphosphine (126 mg, 0.48 mmol, 1.0 equiv) was added THF (4 mL). The reaction mixture was stirred at ambient temperature for 2 h. The solvent was removed under reduced pressure, and the yellow solid dissolved in diethyl ether. The crude solution was then filtered through a pad of Celite, and the solvent reduced until crystal formation began. The solution was placed at −30 °C for 4 h; then pentane was added slowly to the reaction mixture and the solution cooled at −30 °C for an additional 12 h to complete crystallization. The product was isolated by vacuum filtration, washing with cold pentane to give [(PPh$_3$)Pd(CH$_2$C(CH$_3$)$_2$P^{t}Bu$_2$)(OAc)]HOAc (268 mg, 0.389 mmol, 85%) as an off-white crystalline solid.

[(PPh$_3$)Pd(CH$_2$C(CH$_3$)$_2$P^{t}Bu$_2$)(OAc)]HOAc (4). Method B. To a 4 mL borosilicate glass vial charged with complex **1** (74.0 mg, 0.12 mmol) was added triphenylphosphine (35 mg, 0.13 mmol, 1.1 equiv) and THF (2 mL). The reaction mixture was stirred at ambient temperature for 2 h. The solvent was removed under reduced pressure, and the white solid dissolved in diethyl ether. The crude solution was then filtered through a pad of Celite, and the solvent reduced until crystal formation began. The solution was placed at −30 °C for 4 h; then pentane was added slowly to the reaction mixture and the solution

cooled at −30 °C for an additional 12 h to complete crystallization. The product was isolated by vacuum filtration, washing with cold pentane to give [(PPh$_3$)Pd(CH$_2$C(CH$_3$)$_2$P^{t}Bu$_2$)(OAc)]HOAc (75 mg, 0.11 mmol, 93%) as a white crystalline solid. FTIR (film, cm^{-1}): 2963, 2904, 1712, 1602, 1552, 1434, 1255, 1094, 755, 697; ^{1}H NMR (C$_6$D$_6$, 400 MHz): δ 14.21 (s, 1H), 7.86 (t, J = 8.8 Hz, 6H), 7.17−7.14 (m, 6H), 7.08−7.05 (m, 3H), 1.98 (s, 6H), 1.45 (d, J = 13.2 Hz, 18H), 1.22 (d, J = 12.8 Hz, 6H), 0.70 (t, J = 6.8 Hz, 2H). ^{31}P NMR (C$_6$D$_6$, 162 MHz): δ 23.2 (d, J = 402 Hz), 6.0 (d, J = 402 Hz). Anal. Calcd for C$_{34}$H$_{48}$O$_4$P$_2$Pd: C, 59.26; H, 7.02. Found: C, 58.98; H, 7.01.

[(PPh$_2$CH$_2$)$_2$Pd(CH$_2$C(CH$_3$)$_2$P^{t}Bu$_2$)(OAc)]HOAc (5). To a round-bottomed flask charged with complex **1** (92 mg, 0.15 mmol) was added 1,2-bis(diphenylphosphino)ethane (60 mg, 0.15 mmol, 1.0 equiv) and THF (1 mL). The reaction was stirred at ambient temperature for 2 h. After 2 h the solvent was removed under vacuum, and the resulting clear residue was taken up in a minimum amount of toluene, layered with pentane, and placed at −30 °C for 12 h. The off-white crystals were washed with pentane and dried under reduced pressure to give [(Ph$_2$PCH$_2$)$_2$Pd(CH$_2$C(CH$_3$)$_2$P^{t}Bu$_2$)(OAc)]HOAc (118 mg, 0.143 mmol, 98%) as off-white crystals. FTIR (film, cm^{-1}): 3054, 2966, 2911, 1670, 1436, 1367, 1101, 748, 699, 647. ^{1}H NMR (CD$_2$Cl$_2$, 400 MHz): δ 7.57−7.39 (m, 20H), 2.50−2.38 (m, 2H), 2.23−2.13 (m, 2H), 1.789 (s, 6H), 1.44 (d, J = 13.2), 1.21−1.12 (m, 20H). ^{31}P NMR (CD$_2$Cl$_2$, 162 MHz): δ 47.1 (dd, J = 360 Hz, J = 26 Hz), 41.6 (d, J = 26 Hz), −0.5 (d, J = 360 Hz). Anal. Calcd. for C$_{42}$H$_{57}$O$_4$P$_3$Pd: C, 61.13; H, 6.96. Found: C, 61.25; H, 6.84.

Pd(P^{t}Bu$_2$Me)$_2$(OAc)$_2$ (6). Di-*tert*-butylmethylphosphine (P^{t}Bu$_2$Me) (82 mg, 0.51 mmol, 2.3 equiv) was added to a stirring solution of Pd(OAc)$_2$ (50 mg, 0.22 mmol) in THF (1 mL) at 23 °C. The solution was stirred for 2 h. The solvent was removed under reduced pressure, and the resulting yellow solid was dissolved in a minimal amount of diethyl ether, layered with pentane, and placed at −30 °C overnight to promote crystal formation. The product was isolated by vacuum filtration, washing with cold pentane to give Pd(P^{t}Bu$_2$Me)$_2$(OAc)$_2$ (102 mg, 0.153 mmol, 69%) as a yellow crystalline solid. FTIR (film, cm^{-1}): 2966, 2900, 1628, 1370, 1311, 1020, 884, 690. ^{1}H NMR (C$_6$D$_6$, 400 MHz): δ 2.05 (s, 6H), 1.32 (t, J = 6.8 Hz, 32H), 0.89 (t, J = 3.2 Hz, 6H). ^{31}P NMR (C$_6$D$_6$, 162 MHz): δ 28.1. Anal. Calcd for C$_{22}$H$_{48}$O$_4$P$_2$Pd: C, 48.49; H, 8.88. Found: C, 48.45; H, 8.66.

General Procedure for the Reduction of [(P^{t}Bu$_3$)Pd(CH$_2$C(CH$_3$)$_2$P^{t}Bu$_2$)(OAc)]HOAc Using H$_2$. In a 4 mL borosilicate vial with a septum cap, complex **1** (10 mg, 0.16 mmol) was dissolved in toluene-d_8 (1 mL). The reaction mixture was placed under an H$_2$ atmosphere via a balloon of H$_2$ and allowed to purge for 5 min. After the 5 min purge was complete the reaction mixture, under a balloon of H$_2$, was stirred at 23 °C for 12 h. The formation of Pd(P^{t}Bu$_3$)$_3$ was confirmed by ^{1}H NMR and ^{31}P NMR.

General Procedure for the Thermal Reduction of [(P^{t}Bu$_3$)Pd(CH$_2$C(CH$_3$)$_2$P^{t}Bu$_2$)(OAc)]HOAc. In a 4 mL borosilicate vial with septum cap, complex **1** (10 mg, 0.16 mmol) was dissolved in toluene-d_8 (1 mL). The reaction mixture was stirred at 90 °C for 12 h. The formation of Pd(P^{t}Bu$_3$)$_3$ was confirmed by ^{1}H NMR and ^{31}P NMR spectroscopy.

General Procedure for the Amination of 2-Bromotoluene. *N*,*N*-Dibutyl-*o*-toluidine was prepared according to a slightly modified literature procedure as follows.[7] To a 4 mL vial with a septum cap containing 2-bromotoluene (120 μL, 1.00 mmol), dibutylamine (168 μL, 1.00 mmol), sodium acetate (144 mg, 1.50 mmol), 1,3,5-trimethoxybenzene (16.8 mg, 0.100 mmol), and catalyst (0.02 mmol) was added toluene (1 mL). The solution was stirred for 15 min to 6 h at 23, 70, or 110 °C as specified. The reaction solution was then filtered over Celite, and the toluene was removed under vacuum. The resulting residue was taken up in CDCl$_3$ and analyzed by ^{1}H NMR.

General Procedure for the Reduction of Complexes Using NaO^{t}Bu and HNBu$_2$. A 4 mL borosilicate vial was charged with either complex **1** (10 mg, 0.16 mmol), complex **2** (5.0 mg, 0.014 mmol Pd), or a combination of Pd(OAc)$_2$ (10 mg, 0.44 mmol) and P^{t}Bu$_3$ (7.2 mg, 0.36 mmol). Sodium *tert*-butoxide (5 equiv) or sodium *tert*-butoxide (5 equiv) and dibutylamine (5 equiv) were added followed by toluene (1 mL). The resulting mixture was stirred for 1 h before being analyzed by ^{31}P NMR.

■ ASSOCIATED CONTENT

Supporting Information. NMR spectra and X-ray crystallographic data (in CIF format) are available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author
*E-mail: stambuli@chemistry.ohio-state.edu.

■ ACKNOWLEDGMENT

This work was generously supported by The Ohio State University. We thank Dr. Judith Gallucci (OSU) for the X-ray crystal structure of complex **1**.

■ REFERENCES

(1) Wu, X.-F.; Anbarasan, P.; Neumann, H.; Beller, M. *Angew. Chem., Int. Ed.* **2010**, *49*, 9047.
(2) Christmann, U.; Vilar, R. *Angew. Chem., Int. Ed.* **2005**, *44*, 366.
(3) (a) Stambuli, J. P.; Incarvito, C. D.; Bühl, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 1184. (b) Stambuli, J. P.; Bühl, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 9346.
(4) Nishiyama, M.; Yamamoto, T.; Koie, Y. *Tetrahedron Lett.* **1998**, *39*, 617.
(5) Hartwig, J. F.; Kawatsura, M.; Hauck, S. I.; Shaughnessy, K. H.; Alcazar-Roman, L. M. *J. Org. Chem.* **1999**, *64*, 5575.
(6) Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **1999**, *121*, 1473.
(7) Wu, L.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 15824.
(8) (a) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **1998**, *37*, 3387. (b) Littke, A. F.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020.
(9) Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 2719.
(10) (a) Littke, A. F.; Fu, G. C. *J. Org. Chem.* **1999**, *64*, 10. (b) Littke, A. F.; Fu, G. C. *Org. Synth.* **2005**, *81*, 63. (c) Hills, I. D.; Fu, G. C. *J. Am. Chem. Soc.* **2004**, *126*, 13178. (d) Littke, A. F.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 6989.
(11) Hundertmark, T.; Littke, A. F.; Buchwald, S. L.; Fu, G. C. *Org. Lett.* **2000**, *2*, 1729.
(12) (a) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **1999**, *38*, 2411. (b) Littke, A. F.; Schwarz, L.; Fu, G. C. *J. Am. Chem. Soc.* **2002**, *124*, 6343.
(13) Fu, G. C. *Acc. Chem. Res.* **2008**, *41*, 1555.
(14) (a) Russell, C. E.; Hegedus, L. S. *J. Am. Chem. Soc.* **1983**, *105*, 943. (b) Ferroud, D.; Genet, J. P.; Muzart, J. *Tetrahedron Lett.* **1984**, *25*, 4379. (c) Horino, H.; Inoue, N.; Asao, T. *Tetrahedron Lett.* **1981**, *22*, 741. (d) Mulcahy, S. P.; Carroll, P. J.; Meggers, E. *Tetrahedron Lett.* **2006**, *47*, 8877. (e) Fairlamb, I. J. S.; Kapdi, A. R.; Lee, A. F.; McGlacken, G. P.; Weissburger, F.; de Vries, A. H. M.; Schmieder-van de Vondervoort, L. *Chem.−Eur. J.* **2006**, *12*, 8750. (f) Macé, Y.; Kapdi, A. R.; Fairlamb, I. J. S.; Jutand, A. *Organometallics* **2006**, *25*, 1795.
(15) (a) Amatore, C.; Broeker, G.; Jutand, A.; Khalil, F. *J. Am. Chem. Soc.* **1997**, *119*, 5176. (b) Amatore, C.; Jutand, A. *Coord. Chem. Rev.* **1998**, *178−180*, 511. (c) Amatore, C.; Jutand, A.; Khalil, F.; M'Barki, M. A.; Mottier, L. *Organometallics* **1993**, *12*, 3168. (d) Murahashi, S.; Taniguchi, Y.; Imada, Y.; Tanigawa, Y. *J. Org. Chem.* **1989**, *54*, 3292.

(16) Skapski, A. C.; Smart, M. L. *J. Chem. Soc., Chem. Commun.* **1970**, 658b.
(17) (a) Amatore, C.; Jutand, A.; M'Barki, M. A. *Organometallics* **1992**, *11*, 3009. (b) Amatore, C.; Carre, E.; Jutand, A.; M'Barki, M. A. *Organometallics* **1995**, *14*, 1818. (c) Strieter, E. R.; Blackmond, D. G.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 13978. (d) Fors, B. P.; Krattiger, P.; Strieter, E.; Buchwald, S. L. *Org. Lett.* **2008**, *10*, 3505.
(18) (a) Mitchell, E. A.; Baird, M. C. *Organometallics* **2007**, *26*, 5230. (b) Norton, D. M.; Mitchell, E. A.; Botros, N. R.; Jessop, P. G.; Baird, M. C. *J. Org. Chem.* **2009**, *74*, 6674.
(19) (a) Yoshida, T.; Otsuka, S. *J. Am. Chem. Soc.* **1977**, *99*, 2134. (b) Vilar, R.; Mingos, M.; Cardin, C. *J. Chem. Soc., Dalton Trans.* **1996**, 4313. (c) Sommovigo, M.; Pasquali, M.; Leoni, P.; Sabatino, P.; Braga, D. *J. Organomet. Chem.* **1991**, *418*, 119. (d) Goel, R. G.; Montemayor, R. *Inorg. Chem.* **1977**, *16*, 2183. (e) Clark, H. C.; Goel, A. B.; Goel, S. *Inorg. Chem.* **1979**, *18*, 2803.
(20) (a) Geissler, H.; Gross, P.; Guckes, B.; Klimpel, M. German Patent DE19647582A1, 1998. (b) Geissler, H.; Gross, P.; Guckes, B. German Patent DE19647584A1, 1998.
(21) Goel, A. B.; Goel, S.; Vanderveer, D. *Inorg. Chim. Acta* **1981**, *54*, L267.
(22) Herrmann, W. A.; Brossmer, C.; Öfele, K.; Reisinger, C.-P.; Priermeier, T.; Beller, M.; Fischer, H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1844.
(23) (a) Brunel, J. M. *Tetrahedron* **2007**, *63*, 3899. (b) Brunel, J. M. *Synlett* **2007**, *2007*, 0330.
(24) Benazzi, E.; Cameron, C. J.; Mimoun, H. *J. Mol. Catal.* **1991**, *69*, 299.
(25) (a) Menzel, K.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 3718. (b) Hills, I. D.; Netherton, M. R.; Fu, G. C. *Angew. Chem., Int. Ed.* **2003**, *42*, 5749. (c) Kirchhoff, J. H.; Netherton, M. R.; Hills, I. D.; Fu, G. C. *J. Am. Chem. Soc.* **2002**, *124*, 13662. (d) Netherton, M. R.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 3910. (e) Guillou, S.; Janin, Y. L. *J. Heterocycl. Chem.* **2008**, *45*, 1377.
(26) Lee, J.-Y.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 5616.
(27) Kiener, C. A.; Shu, C.; Incarvito, C.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 14272.
(28) (a) Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 1144. (b) Yoo, K. S.; Yoon, C. H.; Jung, K. W. *J. Am. Chem. Soc.* **2006**, *128*, 16384. (c) Lin, B.-L.; Labinger, J. A.; Bercaw, J. E. *Can. J. Chem.* **2009**, *87*, 264. (d) Pattenden, G.; Stoker, D. A. *Synlett* **2009**, *2009*, 1800.
(29) Alcazar-Roman, L. M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 12905.